UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,914	03/02/2004	Fengxia Qi	UAB-17404/22	1392

51279 7590 08/11/2006

GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON & CITKOWSKI, P.C.
P.O. BOX 7021
TROY, MI 48007-7021

EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	10/790,914	QI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/2/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Upon further review, consideration and a pre-appeal conference the finality of the Office action mailed October 19, 2005 has been withdrawn. Claims 9-28 are pending and under examination. The Amendment filed January 19, 2006 has been entered. A Non-Final Office action is submitted below:

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections/Rejection Withdrawn

3. In view of Applicant's amendment and response the following objections and rejections have been withdrawn:

a) objection to claim, page 4 , paragraph 5 of Final Office action.

b) Rejection of claims 17-28 under 35 U.S.C. 112, second paragraph, page 8, paragraph 7 of Final Office action.

Rejection Maintained

4. The rejection under 35 U.S.C 102(b) is maintained for claims 9-10 for the reasons set forth on page 8, paragraph 4 of the previous Office Action.

Loyola-Rodriguez et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract). Loyola-Rodriguez et al teach that mutacin may be a candidate for use in dental caries prevention (see the Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Loyola-Rodriguez et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant's Arguments

Applicant urges that Loyola-Rodriguez et al cannot be used as an anticipatory reference. Applicant urges that mutacin I has a molecular weight of approximately 2364 daltons, is made up of 24 amino acids in mature form and is highly thermostable. Applicant urges that mutacin MT6223 has a molecular weight of 6500 daltons and the chemical structure is unknown. Applicant urges that the fact that claim 9 recites comprising claim language is immaterial and the novelty of that claim over Loyola-Rodriguez et al absent an assertion of how SEQ ID NO:2 is necessarily present in the prior art reference.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed April 19, 2006 have been fully considered but they are not persuasive.

It is the Examiner's position that the prior art teaches the claimed method. It should be remembered that the claims recite open-ended claim language, i.e. "comprising". It should be remembered that the MPEP 2111.03:

The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.");< Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Therefore, the method of treating or preventing a gram-positive infection in a subject used in the prior art administers to subjects a composition which includes an isolated and purified peptide having the amino acid sequence as set forth in SEQ ID NO:2 and other components. The peptide used in the claimed method is isolated and purified from *Streptococcus mutans* and is effective at treating gram-positive infection in a subject. These properties are taught by the peptide of the prior art. SEQ ID NO:2 would be inherent in the teachings of the prior art. It should be remembered the Applicant has not provide a side-by-side comparison of the claimed method with that of

the prior art to show that the methods differ. Therefore, Loyola-Rodriguez et al anticipate the claimed invention.

5. The rejection under 35 U.S.C 112, first paragraph is maintained for claims 9-28 for the reasons set forth on page 4-8, paragraph 6 of the previous Office Action.

The rejections was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claimed invention is directed to methods of treating and preventing gram-positive infections in a subject comprising administering to the subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO 2 or a pharmaceutically acceptable salt, ester or prodrug thereof.

The claimed invention encompasses a method of treating or preventing all gram-positive bacterial infections.

Pages 22-28 of the instant specification describes the isolation and purification of mutacin I. However, the specification fails to disclose methods of treating or preventing any or all gram-positive infections in a subject. Although the specification contemplates the broad spectrum use of mutacin I can be used to treat against a variety of microorganism, the specification fails to teach or disclose data that demonstrates that the amino acid sequence as set forth in SEQ ID NO: 2 can used to provide treatment or protection against infections caused by any or all gram positive microorganisms. There is no disclosure of subjects that have been immunized using the claimed method nor is there a disclosure of challenge studies that have been conducted to established that the amino acid sequence used in the claimed method has the ability to provide protection against any or all gram-positive infections.

The claimed method encompasses treating and preventing infections caused by all gram-positive bacteria. This includes gram-positive bacteria such as *Bacillus anthracis* and *Clostridium botulinum.* O'Brien et al *(American Family Physicians, May 1, 2003, 67, 9)* teach microbes that are used in bioterrorism include *Bacillus anthracis* and *Clostridium botulinum* (page 1928). O'Brien et al teach that familiarity with infectious agents of highest priority can expedite diagnosis and initial management and lead to a successful public health response to a bioterrorist attack (see the Abstract). O'Brien et al has taught that gram-positive bacteria can be quite difficult to diagnosis as well as manage infections caused by these organisms.

The specification has not shown that mutacin I can be used to treat or prevent infections caused by all gram-positive microorganisms. The claimed invention broadly encompasses any infection or disease caused by any gram-positive microorganism.

The claims also broadly encompass all species within the of *Streptococcus, Staphylococcus* or *Enterococcus* genera. Koch et al (*Vaccine 22, 2004, pages 822-830)* teach that the emergence of resistance against multiple antibiotics and the increasing frequency with which *Enterococcus faecalis* and *Enterococcus faecium* are isolated from hospitalization patients underscore the necessity for a better understanding of the virulence mechanisms of this pathogen and the development of alternatives to current antibiotic treatments (see the Abstract). Koch et al teach that enterococci are intrinsically not as virulent as other gram-positive organisms such as *Staphylococcus aureus*, pneumococci or group A streptococci which makes the study of their pathogenicity more difficult (page 822). Koch et al teach that the rapid increase in enterococcal strains resistant to vancomycin and other antibiotics and their ability to pass this trait on to other pathogens, i.e. *Staphylococcus aureus* indicates an urgent and expanding clinical problems (page 822).

It should be noted that the instant specification discloses antimicrobial spectrum assays that with a limited set of pathogens that include *Staphylococcus aureus*, *Staphylococcus epidermidis*, enterococci, pneumocci and Group A streptococci. These studies appear to correlate with *in vitro* studies. The instant specification fails to teach, disclose or correlate the administration of the peptide as set forth in SEQ ID NO:2 (mutacin I) and *in vivo* studies. In other words, the instant specification has failed to disclose administering mutacin I to a subject having a gram-positive bacteria infection and mutacin was successful at treating or preventing the infection. It is unclear from the instant disclosure whether the results from *in vitro* studies can directly correlate to what would be demonstrated *in vivo*.

The above mentioned infections/diseases are only a few of the microorganisms that are encompassed by the claimed invention and represent a small subset of the many diseases that exist that have no vaccine that is effective in treating and/or preventing such infectious diseases. The specification has not shown that mutacin I can be used to treat or prevent infections caused by any gram-positive microorganism much less microorganisms of the genus *Staphylococcus* or *Enterococcus*. The pharmaceutical compositions used in the claimed method would not provide treatment or prevention against any gram-positive bacteria. The specification has not provided enablement for the claimed method since there are no working examples in the instant specification that demonstrate effectiveness of the peptide against all gram-positive microbial infections .nor has the instant specification enabled the use of mutacin I to treat or prevent infections caused by microorganisms of the genera *Staphylococcus* or *Enterococcus*. One skilled in the art would have to possess the knowledge or be provided with sufficient guidance to determine if the pharmaceutical compositions would reach the target microorganisms in order to treat or prevent infection.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect using the amino acid sequence as set forth in SEQ ID NO:2 to treat or prevent all gram-positive infections *in vivo* and 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). It would require undue experimentation by one of skill in the art to determine whether the pharmaceutical compositions used in the claimed method would be effective in treating or preventing any gram-positive microbial infection or disease. One of skill in the art would require guidance, in order to practice the claimed invention in a manner reasonable in correlation with the claims. Without proper guidance, the experimentation is undue.

Applicant's Arguments

A) Applicant urges that the claimed invention is fully enabled. Applicant urges that the invention involves the treatment and prevention of gram-positive infection via a step of administering an effective amount of the isolated and purified peptide as set forth in SEQ ID NO:2. Applicant urges that the instant specification at pages 12-21 teaches the administration of SEQ ID NO:2 and the spectrum of efficacy is submitted to cover enough varied bacterial genuses to support claim 9. Applicant urges that claim 17 has a narrower infective indication of staphylococci, enterococci and pneumococci.

B) Applicant urges that testing the susceptibility of a particular microorganism to an inventive peptide is well within the talents of one skill in the art. Applicant refers to Loyola-Rodriguz et al for an exemplary teaching with respect to Table 2 of methodologies for measuring the level of success. Applicant urges that one skilled in

the art certainly has the ability to test susceptibility of these pathogens towards an inventive composition without undue experimentation.

C) Applicant urges that the efficacy of a given medical treatment has long been held to reside within the purview of the Food and Drug Administration and not the Patent Office.

D) Applicant urges that the un-entered declaration submitted by Dr. Caufield indicates that the peptide as set forth in SEQ ID NO:2 is effective against a variety of gram-positive bacteria including *S. pyogenes, S. pneumoniae*, multiple drug resistant *Staphylococcus aureus*, vancomycin –resistant *E. faecium* and *Bacillus anthracis*.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed April 19, 2006 have been fully considered but they are not persuasive.

A) It is the Examiner's position that the claimed invention is not enabled by the instant specification. It should be remembered that independent claim 9 encompasses all gram-positive bacteria. The instant specification has not provided enablement to treat or prevent all gram-positive bacteria infections. Pages 12-21 of the instant specification does not enable the treatment or prevention of all gram-positive infections. The instant specification has provide no experimental examples to demonstrated that the claimed method can be used to treat or prevent all gram-positive bacteria. The instant specification merely makes the statement the ".... Mutacin III is more potent than

mutacin I against *S. aureus* and *S. epidermidis* while both mutacins have equal activities against other pathogens such as enterococci, pneumococci and Group A streptococci" (page 33). It noted that the pathogens such as enterococci, pneumococci and Group A streptococci do not cover the broad spectrum of all gram-positive bacteria other genera such as *Clostridium*, *Bacillus* and *Listeria*. It should be noted that the claims also recite "prevention of gram-positive infection". It should be remembered that the term "prevention" or "preventing" encompasses the ability of the specific antigen to induce protective immunity to all gram-positive infection or disease induction. The specification does not provide substantive evidence that the peptides used in the claimed method are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed method for its intended purpose of preventing all gram-positive infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the peptides used in the claimed, i.e. would not be able to accurately predict if protective immunity has been induced.

B) To address Applicant's arguments regarding testing the susceptibility of a particular microorganism to an inventive peptide, it should be remembered that 112 first paragraph requires that the instant specification teach how to "make and use" the claimed invention and not "how to find out how to use the claimed method". Although it is known in the art to test or measure the success of inventive peptide, i.e. administration of SEQ ID NO:2, the instant specification has not demonstrated that the peptide set forth in SEQ ID NO:2 is effective in treating and preventing all gram-positive

bacterial infections. It is the Examiner's position that it would require undue experimentation to practice (make and use) the claimed invention based on the teaching found in the instant specification.

C) To address Applicant's comments regarding the efficacy of medical treatment, it should be noted that the U.S. Patent Office has a responsibility to assure that the claimed invention satisfies the requirements under 35 U.S.C. 112, first paragraph.

D) The Declaration submitted by Dr. Caufield is insufficient to overcome this rejection. The Declaration submitted by Dr. Caufield, it appears to disclose inhibition assays (*in vitro* assays) were preformed using, *S. pyogenes, S. pneumoniae*, multiple drug resistant *Staphylococcus aureus*, vancomycin –resistant *E. faecium* and *Bacillus anthracis*. It should be noted that Appendix A submitted with the declaration lacks clarity since the photocopies of the results of inhibition assays are unclear. However, this declaration only encompasses a few species within *the Staphylococcus, Streptococcus, Enterococcus* and *Bacillus* genera and not all species or strains within these genera as encompassed by claim 17. Nor does the data submitted in Appendix A include all gram-positive bacteria as encompassed by claim 9.

The Declaration submitted by Dr. Caufield has failed to provide a correlation between *in vitro* studies and what would be demonstrated *in vivo*. The declaration as well as the instant specification has failed teach or disclose a method of treating or preventing gram-positive infection in a subject (*in vivo*) by administering mutacin I (SEQ ID NO:2) and then challenging the subject to see what level of protection (preventing) or treatment can be obtained. This limitations are requirements of the claimed method.

Without this demostration, Applicant has not met his burden under 35 U.S.C. 112, first paragraph.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification teaches that the terms "pharmaceutically acceptable salts, esters, amides and prodrugs" as used herein refers to these carboxylate salts, amino acid addition salts, esters, amides and prodrugs of the compounds of the present invention (page 19). *MedicineNet.com* (http://www.medterms.com/script/main/art) (accessed 8/3/06) defines a prodrug as a precursor or forerunner of a drug that must undergo a chemical conversion. Thus, it can be concluded that a prodrug has a different structure than the isolated and purified protein as set forth in SEQ ID No:2

(mutacin I). The Examiner is interpreting the term "prodrug" to mean variant of SEQ ID NO:2.

As stated in the previous rejection under 35 U.S. 112, first paragraph, the instant specification has failed to enable a method of treating or preventing a gram-positive infection in a subject by administering mutacin I (SEQ NO:2) or a prodrug of SEQ ID NO:2 to the subject.

There is no guidance provided as to which amino acids can be modified and the polypeptide would retain its biological function. The variant or prodrug of the claims encompasses an extremely large number of polypeptides. The instant specification has not taught a prodrug of SEQ ID NO: 2 or how to use it in the claimed method. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation. There is no guidance as to what amino acids may not be changed without causing a detrimental effect to the polypeptide being claimed. The claims broadly teach polypeptides which

include amino acid additions, substitution or combinations thereof. Therefore any polypeptide is being claimed, and no specific location for which the modification can be made.. Thus, the resulting polypeptide could result in a polypeptide not taught nor enabled by the specification.

Thomas E. Creighton, in his book, "*Proteins: Structures and Molecular Properties, 1984",* (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes: 1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a proline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "*Protein Structure: A Practical Approach, 1989; pages 184-186"* teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in *"Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph)* adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins

appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Therefore the specification fails to provide guidance regarding as how to make the peptides used in the claimed method. One of skill in the art would require guidance, in order to make or use "produgs" in a manner reasonable in correlation with the scope of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting terms "produgs" having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to practice (make and use) the recited terms "prodrugs" in a manner reasonable in correlation with the claims. Without proper guidance, the experimentation is undue.

Claim R jections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ikeda et al *(Infection and Immunity, 1982, Vol. 35, No. 3, p. 861-868)*.

Claims 9-10 are directed to a method of treating or preventing an infection in a subject said method comprising administering to said subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO: 2 or a pharmaceutical acceptable salt, amide, ester or prodrug thereof.

Ikeda et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract and page 863). Ikeda et al teach that when water or diet containing the bacteriocin from Streptococcus mutans was administered to animals the caries score of these animals was found to be significantly reduced (see the Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Ikeda et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material

method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ooshima et al *(Microbiol. Immunol., Vol. 29 (12), 1163-1173, 1985).*

Claims 9-10 are directed to a method of treating or preventing an infection in a subject said method comprising administering to said subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO: 2 or a pharmaceutical acceptable salt, amide, ester or prodrug thereof.

Ooshima et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract and page 863). Ooshima et al teach that when water or diet containing the bacteriocin from Streptococcus mutans was administered to animals the dental caries of these animals was found to be significantly reduced (see the Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Ikeda et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status f Claims

9. No claims allowed.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vanessa L. Ford
Biotechnology Patent Examiner
August 1, 2006

NITA MINNIFIELD
PRIMARY EXAMINER